
Stem cell gene expression programs influence clinical outcome in human leukemia.

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Public Summary:

Xenograft studies indicate that some solid tumors and leukemias are organized as cellular hierarchies sustained by cancer stem cells (CSCs). Despite the promise of the CSC model, its relevance in humans remains uncertain. Here we show that acute myeloid leukemia (AML) follows a CSC model on the basis of sorting multiple populations from each of 16 primary human AML samples and identifying which contain leukemia stem cells (LSCs) using a sensitive xenograft assay. Analysis of gene expression from all functionally validated populations yielded an LSC-specific signature. Similarly, a hematopoietic stem cell (HSC) gene signature was established. Bioinformatic analysis identified a core transcriptional program shared by LSCs and HSCs, revealing the molecular machinery underlying 'stemness' properties. Both stem cell programs were highly significant independent predictors of patient survival and were found in existing prognostic signatures. Thus, determinants of stemness influence the clinical outcome of AML, establishing that LSCs are clinically relevant and not artifacts of xenotransplantation.

Scientific Abstract:

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